

Research paper

Treating depressive disorders with the Unified Protocol: A preliminary randomized evaluation



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ABSTRACT

Objectives: This study aims to examine the efficacy of the Unified Protocol for Transdiagnostic Treatment of Emotional Disorders (UP) for individuals diagnosed with a depressive disorder.

Method: Participants included 44 adults who met criteria for major depressive disorder, persistent depressive disorder, or another specified depressive disorder according to the Anxiety Disorder Interview Schedule (ADIS). These individuals represent a subset of patients from a larger clinical trial comparing the UP to single-disorder protocols (SDPs) for discrete anxiety disorders and a waitlist control (WLC) condition (Barlow et al., 2017); inclusion criteria for the parent study required participants to have a principal anxiety disorder.

Results: Significant reductions in depressive symptoms were observed within the UP condition across clinician-rated and self-report measures of depression from baseline to post-treatment, as well as to the 12-month follow-up assessment. Compared to the WLC group, individuals in the UP condition demonstrated significantly lower levels on our continuous, clinician-rated measure of depressive symptoms at post-treatment. There were no differences between the UP and SDP conditions on depressive symptoms at post-treatment or at the 12-month follow-up timepoint.

Conclusions: In this exploratory set of analyses, the UP evidenced efficacy for reduction of depressive symptoms, adding to the growing support for its utility in treating depression.

1. Introduction

The Unified Protocol for the Transdiagnostic Treatment of Emotional Disorders (UP) (Barlow et al., 2011, 2018) is an emotion-focused, cognitive-behavioral treatment designed to target core temperamental factors that underlie the development and maintenance of anxiety, depressive, and related disorders (i.e., emotional disorders; Bullis et al., 2019). These core factors include the propensity to experience frequent and intense negative affect, coupled with aversive reactions to emotional experiences when they occur (Barlow et al., 2014). The UP aims to reduce both the perception of negative affect as intolerable, as well as the avoidant coping strategies that result from these beliefs (Farchione et al., 2012). Importantly, this transdiagnostic framework may have advantages for the dissemination of evidence-based treatment. By emphasizing the shared mechanisms that underlie

emotional disorders, rather than surface-level symptoms of specific disorders (e.g., panic, worry, social evaluation concerns, low mood), the UP has the potential to reduce burdens associated with training clinicians in many “diagnosis-specific” treatments; indeed, the UP represents a single protocol that can be flexibly used to target a broad range of comorbid conditions (e.g., Barlow et al., 2017a).

To date, the majority of efficacy data for the UP exist for individuals with anxiety disorders. Initial findings suggest that the UP results in significant improvement for symptoms of anxiety and depression in individuals with heterogeneous anxiety disorders (Ellard et al., 2010; Farchione et al., 2012). Recently, in a large randomized controlled trial (RCT), Barlow et al. (2017) demonstrated that the UP resulted in equivalent symptom reduction for principal anxiety disorders as gold-standard single-disorder cognitive-behavioral protocol (SDP) explicitly developed to target each individual condition (Barlow et al., 2017);

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further, those in the UP condition were more likely to remain in treatment longer than individuals in SDPs (Barlow et al., 2017).

1.1. Applicability of the UP for depression

Though the UP has been most widely studied for anxiety disorders, converging theory and empirical evidence also indicate the promise of using this transdiagnostic approach to treat depression. Depressive disorders are highly comorbid with anxiety disorders (e.g., Brown and Barlow, 1992; Brown et al., 2001; Fava et al., 2000; Kessler et al., 1996), and researchers have theorized that shared vulnerabilities underlying depressive and anxiety disorders may be the reason for these high comorbidity rates (Andrews, 1996, 1990; Barlow et al., 2014). Indeed, empirical work supports the notion that neuroticism accounts for substantial variation in emotional disorders (e.g., Brown et al., 1998, 2007; Brown and Barlow, 2009; Griffiths et al., 2010; Kasch et al., 2002; Kessler et al., 2011), and that this trait is elevated in individuals with MDD (Brown and Rosellini, 2011; Clark and Watson, 1991). As noted above, the transdiagnostic UP was specifically designed to target neuroticism, and thus, should be applicable across all disorders (including multiple comorbidities and symptoms) for which this trait plays a key role. Given that depression is highly prevalent, affecting 7% of the population (Brody et al., 2018), and is associated with significant societal costs (Greenberg et al., 2015), it is necessary to continue to establish effective treatments for this condition.

The core treatment components of the UP are highly relevant to depression. Briefly, intense and frequent negative affect (e.g., sadness, guilt, anger) and maladaptive, avoidant reactions to negative affect (e.g., social withdrawal, hypersomnia) characterize depression; as previously noted, intense and frequent negative affect and aversive responding to negative affect are the UP's primary (transdiagnostic) intervention targets. Furthermore, the UP also shares many key therapeutic strategies with extant empirically supported interventions for depression. For example, the first module incorporates motivational interviewing techniques that have been shown to improve treatment for individuals with depressive disorders (Keeley et al., 2016). Additionally, the second and third UP modules focus on cultivating a more objective, approach-oriented stance toward emotions - akin to mindfulness- and acceptance-based approaches for depression (Segal et al., 2002; Goldberg et al., 2018). The UP's fourth module focuses on identifying automatic appraisal patterns and teaching cognitive reappraisal strategies to generate alternative cognitions, similar to traditional cognitive and cognitive-behavioral treatments for depression, while continuing to emphasize nonjudgmental awareness of one's thoughts. In the UP's "behavioral" module (the fifth module), like existing behavioral activation treatments for depression, patients practice identifying and modifying maladaptive, avoidant responses (e.g., inactivity, withdrawal) with specific, approach-oriented behaviors. Last, the sixth and seventh modules consist of systematic exposure exercises, in line with the many cognitive-behavioral treatment protocols for depression that incorporate behavioral experiments as a key procedure.

1.2. Prior evidence of the UP for depression

Preliminary empirical support of the UP for patients with unipolar depressive disorders comes from single-case and case studies, as well as small open-label and controlled trials of patients with co-occurring depressive disorders (and in some cases, principal MDD). For example, Boswell et al. (2014) reported on changes in symptoms and putative mechanisms of change over the course of UP treatment in a 64-year-old female with a principal diagnosis of MDD, along with recurrent and co-occurring generalized anxiety disorder (GAD). Several additional case studies of individual patients with MDD who were treated with the UP have additionally shown clinically significant or reliable changes in self-reported depressive symptoms (Boswell and Bugatti, 2016; Boswell et al., 2018; Farchione et al., 2017; Hague et al., 2015).

In one of the first trials of the UP for patients with anxiety ($N = 18$, $n = 3$ of whom had comorbid depression), significant, moderate effects of the UP on clinician-rated depressive symptoms were observed in the overall sample (Ellard et al., 2010). Though reductions in clinician-rated and self-report indicators of scores of depressive disorder severity were not statistically significant, the three patients who met criteria for a depressive disorder at baseline were all classified as "responders" (for their depressive disorder) at six-month follow-up. In a later open trial of the UP in Japan for adults with unipolar depression or anxiety (53% had principal depression), medium to large, significant reductions in depression were shown (Ito et al., 2016). Similar results were observed when the UP was delivered in group format in the Spanish public health system (Osma et al., 2015). In the first randomized, waitlist-controlled trial of the UP for adults with anxiety disorders ($N = 37$), 6 of 9 patients with a co-occurring depressive disorder no longer met criteria for depression at post-treatment, and at a six-month follow-up, 8 of 9 patients no longer met depressive disorder criteria (Farchione et al., 2012); large, statistically significant effect sizes for both clinician-rated and self-report measures of depression favored the UP. Similar results, favoring the UP versus a waitlist control condition, have also been found in a sample of patients ($N = 29$) with bipolar I or II experiencing a depressive episode (Ellard et al., 2017).

1.3. Applicability and preliminary evidence for suicidal ideation

As one of the nine symptoms of MDD (American Psychiatric Association, 2013), suicidal ideation may also be effectively targeted with the UP. As detailed in Bentley et al. (2017b), leading theoretical models point to the experience of intense negative affect as a key factor in the development and maintenance of suicidal thoughts and behaviors (e.g., Baumeister, 1990; Beck, 1986; Joiner, 2007; Linehan 1993; Shneidman, 1993); indeed, neuroticism is associated with suicidal ideation even when adjusting for comorbid clinical disorders (e.g., Handley et al., 2012; Mandelli et al., 2015; Rappaport et al., 2017). Additionally, clinical observation (e.g., O'Connor, 2003; Selby et al., 2007) and initial empirical support (e.g., Kleiman et al., 2018) suggest that suicidal thoughts and behaviors may serve similar functions to the aversive, avoidant reactions to negative affect that maintain emotional disorders. Whereas contemplating ending one's life to relieve or escape intense emotional pain (or making a suicide plan or engaging in suicidal behavior) may provide some short-term relief from extremely distressing emotional states or comfort (e.g., Crane et al., 2014), these behaviors are unlikely to lead to long-term relief and may even worsen negative emotions over time (e.g., Crowell et al., 2014). Last, ample research has demonstrated that suicidal ideation and emotional disorders frequently co-occur (e.g., Nock et al., 2010; Nock et al., 2009; Zimmerman et al., 2014). Pilot studies exploring the utility of the UP for addressing suicidal thoughts and behaviors have demonstrated that this approach is feasible, acceptable to patients, and is associated with promising improvements (Bentley et al., 2017a).

1.4. The present study

The present study is a secondary analysis of a recently completed clinical equivalency trial comparing the UP to gold-standard cognitive-behavioral protocols designed to target a single discrete anxiety diagnosis (i.e., SDP), along with a waitlist control (WLC) condition (Barlow et al., 2017). We previously described changes in clinician-rated and self-reported depressive symptoms for *all* patients (i.e., with and without a co-occurring depressive disorder) in the UP condition ($N = 88$) and observed significant differences at post-treatment favoring the UP in comparison to the WLC, and non-significant differences compared to the SDPs (Barlow et al., 2017).

Here we expand upon previous findings by exploring the effects of the UP on depression in individuals with principal anxiety disorders who also met criteria for a unipolar depressive disorder. The subset of

44 patients meeting this criterion were drawn from the larger trial, representing the largest sample of patients with a depressive disorder included in a randomized UP trial to date. Specifically, we explore changes in depressive symptoms for the individuals with a comorbid unipolar depressive disorder who received the UP ($n = 17$) from pre- to post-treatment and 12-month follow-up. Additionally, we evaluate whether levels of depression between individuals treated with UP versus those in the waitlist condition ($n = 12$) are significantly different at pre-treatment and post-treatment. We also compare levels of depression between the UP and SDP ($n = 15$) conditions at pre- and post-treatment, along with at the 6-month follow-up. Finally, as an additional exploratory aim, we also explore changes in suicidal ideation during across available study timepoints for each condition.

2. Method

2.1. Participants

Treatment-seeking participants from the community were recruited from a large, university-based community mental health center at Boston University. English-speaking adults with a principal (most interfering and severe) diagnosis of panic disorder (PD), generalized anxiety disorder (GAD), obsessive-compulsive disorder (OCD), or social anxiety disorder (SOC), as assessed by the Anxiety Disorders Interview Schedule (ADIS; Brown and Barlow, 2014; Brown et al., 1994), were eligible. In line with long standing procedures for clinical trials at our Center, individuals taking psychotropic medications were required to have been stable on the same dose for at least six weeks prior to enrollment, and to maintain these medications and dosages throughout the treatment. Exclusion criteria consisted primarily of conditions that required prioritization for immediate or simultaneous treatment that could interact with the study treatment. For more information, see Barlow et al. (2017).

A total of 223 participants in the parent clinical trial (see Barlow et al., 2017) were randomized in a 2:2:1 allocation ratio to the following three conditions: UP, SDP,¹ and waitlist control (WLC). Given our goal of evaluating the UP's effect on depressive symptoms, the present study includes the subset of participants who reached clinical severity ratings (CSR) of four or higher for a depressive disorder at baseline ($n = 44$), reflecting a clinical level of distress/impairment associated with their depressive disorder specifically (see diagnostic assessment section below; Brown and Barlow, 2014). The sample was predominantly white (77.27%), female (47.73%), with a mean age of 33.36 ($SD = 11.71$) and had attended at least some college (93.18%).

2.2. Procedures

Patients in the UP and SDP conditions completed a 16-session acute treatment phase, followed by a 12-month follow-up phase; of note, patients with principal PD/A received 12 sessions to match the treatment length recommendations for the SDP condition (see Study Intervention section for full details on each SDP). Patients in the WLC condition completed 16-week assessment-only phase after which their study participation was completed; WLC patients did not participate in the follow-up phase. In the context of the present study, participants in all conditions completed self-report questionnaires and clinician-rated assessments at pre- and post-treatment; participants in the UP and SDP conditions were also assessed at the 12-month follow-up time-point. Clinician rated assessments were conducted by independent evaluators

¹ Patients assigned to this condition received a manualized, single diagnosis protocol that was associated with their principal diagnosis. For example, patients assigned to this condition with PD/A received Mastery of Your Anxiety and Panic (Barlow & Craske, 2007), whereas patients with GAD received Mastery of Your Anxiety and Worry (Craske & Barlow, 2006).

were trained to reliability on study instruments and were blinded to study condition. All procedures were approved by Boston University's Institutional Review Board and patients provided their informed consent before participating.

2.3. Study interventions

The UP was delivered in accordance with the published materials (Barlow et al., 2011, 2018). The UP consists of five core treatment modules: (1) Mindful Emotion Awareness; (2) Cognitive Flexibility; (3) Countering Emotional Behaviors; (4) Awareness and Tolerance of Physical Sensations; and (5) Emotion Exposures. Sessions for patients with GAD, PD/A, and SOC were 60 min in duration, whereas patients with OCD received 90-minute sessions to correspond to the length recommendations made by the SDP for this disorder (see below for full information about each SDP).

The SDP treatment protocols adopted in the present study included: Mastery of Anxiety and Panic – 4th edition (MAP-IV; Craske and Barlow, 2006); Treating Your OCD with Exposure and Response (Ritual) Prevention Therapy – 2nd edition (ERP-II; Foa et al., 2012); Mastery of Anxiety and Worry – 2nd edition (MAW-II; Zinbarg et al., 2006); and Managing Social Anxiety: A Cognitive-Behavioral Therapy Approach – 2nd edition (MSA-II; Hope et al., 2010). As noted previously, treatment consisted of 16 sessions, each 60-minutes in duration, with the exception of the OCD intervention (90-minute session) and the PD/A protocol (12 sessions).

2.4. Therapists and treatment integrity

Study therapists were doctoral students in clinical psychology, postdoctoral fellows, and licensed clinical psychologists with training and certification in the treatment protocols utilized (Barlow et al., 2000). For both the UP condition and the SDPs, expert raters associated with the development of each treatment provided an overall competence rating for 20% of study sessions; these ratings incorporated adherence to a checklist of topics to be covered in each session, along with basic therapeutic skills (e.g., built rapport, demonstrates empathy). Competence scores sessions were high in both the UP (mean: 4.44 out of 5) and SDP (mean: 4.09 out of 5) conditions.

2.5. Measures

In order to provide a comprehensive understanding of the UP's effects on depression, the present study includes three unique indicators of this condition. These measures are, of course, related, though correlations ($r = 0.55 - 0.61$) suggest they are not entirely overlapping (Bentley et al., 2014; Gallagher et al., 2013)

Diagnostic assessment. Blinded study evaluators used a semi-structured clinical interview, the Anxiety Disorders Interview Schedule (ADIS; Brown and Barlow, 2014), to assess patients for current DSM diagnoses. Diagnoses are assigned a clinical severity rating (CSR) on a scale from 0 to 8; ratings of 4 or above indicate that a patient meets clinical threshold for the diagnosed disorder and, as noted previously, individuals with ratings above 4 for any depressive disorder were included in the present study. ADIS CSR scores represent clinician impressions of overall distress and impaired experienced as a function of a particular mental health conditions. These ratings are transdiagnostic (i.e., are on the same scale across disorders assessed by the ADIS), allowing us to explore changes in CSR for MDD specifically, as well as for any depressive disorder. As reported in the parent trial, inter-rater agreement was 98% for principal diagnosis ADIS CSR, following criteria specified by Brown et al. (2001).

Clinician-rated. The Hamilton Depression Rating Scale (HAM-D; Hamilton, 1960) is a 17-item widely used measure of depressive symptoms administered by independent evaluators in accordance with the Structured Interview Guide for the Hamilton Depression Rating

Scale (SIGH-D; Williams, 1988). In the present study, HAM-D scores represent clinician-rated impressions of symptom severity. The measure includes one item (item 11) evaluating suicidal thoughts and behaviors, made up of the following questions “This past week, have you had any thoughts that life is not worth living, or that you would be better off dead?,” “What about having thoughts of hurting or even killing yourself?,” and “Have you actually done anything to hurt yourself?” Responses are categorized in terms of severity from 0 to 6 (0 = absent, 1 = feels life is not worth living, 2 = wishes to be dead or has any thoughts of possible death to self, 3 = suicidal ideas or gestures, 4 = attempts at suicide). As reported in the parent trial, inter-rater agreement for the HAM-D was 0.92.

Self-report. The Overall Depression Severity and Impairment Scale (ODSIS; Bentley et al., 2014) is a measure adapted from the Overall Anxiety Severity and Impairment Scale (OASIS; Norman et al., 2006) to briefly assess depression severity and impairment. The ODSIS asks about depressive symptoms in the past week, and scores range from 0 to 20 with a clinical cutoff of 8. The ODSIS has established good internal consistency, convergent validity, and discriminant validity (Bentley et al., 2014). In this sample, $\alpha = 0.87$ at baseline.

3. Results

With regard to depressive diagnoses, across the three treatment conditions, 31 patients met criteria for major depressive disorder, 12 met criteria for dysthymia (DSM-IV) or persistent depressive disorder (DSM-5), 6 met criteria for not-otherwise specified depressive disorder (DSM-IV)/other specified depressive disorder (DSM-5). In several instances, individuals met criteria for more than one depressive disorder; thus the number of discrete depressive disorders exceeded the total N. See Table 1 for a breakdown of depressive diagnoses with each principal anxiety disorder category included in the parent study, along with as a function of treatment condition. The mean CSR at baseline for any depressive disorder in this sample was 4.61, suggesting moderate symptoms and interference. Additionally, there were no significant differences in CSR (Hedge's $g = 0.30$, $[-0.39, 0.99]$), HAM-D ratings (Hedge's $g = 0.44$, $[-0.31, 1.19]$), or ODSIS (Hedges's $g = 0.73$, $[-0.16, 1.62]$) scores at baseline between patients in UP and WLC conditions at baseline. Similarly, there were no pre-treatment

Table 1
Breakdown of depressive disorder occurrence within principal anxiety diagnoses.

Depressive diagnosis	Principal Anxiety Disorder			
	PD/A	SOC	GAD	OCD
MDD				
UP $n = 12$	$n = 2$	$n = 5$	$n = 4$	$n = 1$
SDP $n = 9$	$n = 1$	$n = 2$	$n = 5$	$n = 1$
WLCn = 10	$n = 1$	$n = 2$	$n = 5$	$n = 2$
Total $n = 31$	$n = 4$	$n = 9$	$n = 14$	$n = 4$
PDD/DYS				
UP $n = 7$	$n = 1$	$n = 1$	$n = 1$	$n = 4$
SDP $n = 2$	$n = 1$	$n = 1$	$n = 0$	$n = 0$
WLCn = 3	$n = 0$	$n = 1$	$n = 0$	$n = 2$
Total $n = 12$	$n = 2$	$n = 3$	$n = 1$	$n = 6$
Total DDNOS/OS DD				
UP $n = 1$	$n = 0$	$n = 0$	$n = 0$	$n = 1$
SDP $n = 4$	$n = 1$	$n = 2$	$n = 0$	$n = 1$
WLCn = 1	$n = 0$	$n = 0$	$n = 1$	$n = 0$
Total $n = 6$	$n = 1$	$n = 2$	$n = 1$	$n = 2$

Note: PD/A = Panic disorder with/without agoraphobia, SOC = social anxiety disorder, GAD = generalized anxiety disorder, OCD = obsessive compulsive disorder, MDD = major depressive disorder, PDD = persistent depressive disorder, DYS = dysthymia, DDNOS = not-otherwise specified depressive disorder, and OS DD = other specified depressive disorder. UP = Unified Protocol, SDP = Single Disorder Protocol, WLC = Waitlist Control.

differences in depression scores between the UP and SDP in CSR (Hedge's $g = -0.16$, $[-1.02, 0.71]$), HAM-D ratings (Hedge's $g = 0.31$, $[-0.39, 1.01]$), or ODSIS (Hedges's $g = 0.55$, $[-0.16, 1.26]$).

Descriptive data and within condition effect sizes for the UP, WLC, and SDP conditions at all available time points can be viewed in Table 2. Means for all depression variables changed in the expected direction across treatment with the UP; specifically, mean CSR (for any depressive disorder and MDD, in particular), HAM-D ratings, and ODSIS scores decreased from baseline to post-treatment, and continued improvement was observed at the 12-month follow-up assessment. Within-condition standardized mean gain effect sizes (ES_{sg}) revealed that these changes from baseline to the 12-month follow-up were large in magnitude and statistically significant (indicated by confidence intervals not overlapping zero) in the UP.

In contrast, across CSRs, HAM-D ratings, and ODSIS scores, depressive symptoms did not improve significantly for WLC from pre- to post-treatment. Between-condition effect sizes comparing patients in the UP and WLC conditions at post-treatment revealed significant differences in HAM-D ratings favoring the UP that were large in magnitude (Hedge's $g = -1.11$, $[-2.07, -0.15]$). Medium to large differences were also observed between UP and WLC conditions for CSRs (any depressive disorder; Hedge's $g = -0.77$, $[-1.64, 0.09]$) and ODSIS scores (Hedge's $g = -1.07$, $[-2.17, 0.03]$) at post-treatment, though these effects only approached significance (Fig. 1).

Means across study time-points, along with within-condition effect sizes, revealed that the SDP condition exhibited a similar pattern of change in depressive symptoms to the UP condition; specifically, SDP patients demonstrated statistically significant improvements in clinician-rated and self-reported symptoms of depression, that were large in magnitude; changes in diagnostic severity (i.e., ADIS CSR) were not statistically significant (though they were in the UP condition). Additionally, there were no statistically significant differences in CSR for any depressive disorder (Hedge's $g = 0.48$, $[-0.37, 1.33]$), HAM-D ratings (Hedge's $g = 0.28$, $[-0.56, 1.12]$), or ODSIS (Hedges's $g = 0.30$, $[-0.57, 1.17]$) between the UP and SDP conditions at post-treatment or at the 12-month follow-up assessment (CSR: Hedge's $g = 0.43$, $[-1.39, 1.24]$; HAM-D: Hedge's $g = 0.31$, $[-0.34, 1.24]$; ODSIS: Hedges's $g = 0.26$, $[-0.56, 1.08]$).

Additionally, a more in-depth investigation on the effect of the UP on suicidal ideation (as a core symptom of depression) was conducted. Specifically, we examined the frequency of non-zero responses to item 11 on the HAM-D. In the UP condition, 8 individuals endorsed a value of at least one on this item at baseline; scores ranged from 1 to 3, indicating that suicidal ideation in our sample ranged from beliefs that life is not worth living ($n = 6$), to thoughts of death and dying ($n = 1$), to intent and/or an expressed plan ($n = 1$). At post-treatment, one individual reported feeling that life is not worth living (i.e., score of 1 on HAM-D item 11), and at the 12-month follow-up, no patients endorsed this item. Similarly, in the SDP condition, four individuals endorsed a value of one (beliefs that life is not worth living) on this item at baseline. At post-treatment, one individual reported feeling that life is not worth living (i.e., score of 1 on HAM-D item 11), and at the 12-month follow-up, no patients endorsed this item. In contrast, in the WLC condition, 2 individuals expressed feelings that life is not worth living at baseline, whereas 1 patient responded this way at the end of the waitlist period. Given the low base rate for these responses, subsequent statistical tests were not conducted. In summary, however, within both the UP and SDP conditions, the frequency and severity of suicidal item endorsement decreased in the expected direction across treatment and into the follow-up phase.

4. Discussion

The current study explored the effects of treatment with the UP on depressive symptoms and suicidal ideation for patients with a principal anxiety disorder who also met criteria for at least one unipolar

Table 2
Means and within-condition effect sizes at all available study timepoints.

	Treatment group	Means Pre	Post	12MFU	Pre-post effect size change	Pre-12MFU effect size change
MDD CSR	UP	<i>M</i> = 4.58 <i>n</i> = 12 SD = 0.51	<i>M</i> = 2.63 <i>n</i> = 8 SD = 1.60	<i>M</i> = 1.63 <i>n</i> = 8 SD = 1.19	ES _s g = 1.63(large) CI[0.42,2.83]	ES _s g = 3.29(large) CI[1.39,5.18]
	SDP	<i>M</i> = 4.67 <i>n</i> = 9 SD = 0.50	<i>M</i> = 2.20 <i>n</i> = 5 SD = 2.05	<i>M</i> = 2.00 <i>n</i> = 6 SD = 2.19	ES _s g = 1.50(large) CI[-0.09,3.09]	ES _s g = 1.76(large) CI[-0.01,3.53]
	WLC	<i>M</i> = 4.60 <i>n</i> = 10 SD = 0.70	<i>M</i> = 4.33 <i>n</i> = 6 SD = 1.37		ES _s g = 0.34(small) CI[-0.15,0.82]	
Any DD CSR	UP	<i>M</i> = 4.70 <i>n</i> = 20 SD = 0.66	<i>M</i> = 2.93 <i>n</i> = 14 SD = 1.38	<i>M</i> = 2.08 <i>n</i> = 13 SD = 1.32	ES _s g = 1.60(large) CI[0.73,2.48]	ES _s g = 2.62(large) CI[1.36,3.88]
	SDP	<i>M</i> = 4.36 <i>n</i> = 14 SD = 1.34	<i>M</i> = 2.11 <i>n</i> = 9 SD = 1.96	<i>M</i> = 1.36 <i>n</i> = 11 SD = 1.91	ES _s g = 1.68(large) CI[0.49,2.86]	ES _s g = 2.36(large) CI[0.88,3.83]
	WLC	<i>M</i> = 4.50 <i>n</i> = 14 SD = 0.65	<i>M</i> = 4.11 <i>n</i> = 9 SD = 1.62		ES _s g = 0.35 (small) CI [-0.19, 0.89]	
HAM-D	UP	<i>M</i> = 19.59 <i>n</i> = 17 SD = 7.27	<i>M</i> = 8.61 <i>n</i> = 12 SD = 6.52	<i>M</i> = 7.75 <i>n</i> = 12 SD = 7.36	ES _s g = 1.72 (large) CI [0.68, 2.76]	ES _s g = 1.43 (large) CI [0.50, 2.37]
	SDP	<i>M</i> = 17.40 <i>n</i> = 15 SD = 6.40	<i>M</i> = 6.76 <i>n</i> = 10 SD = 6.21	<i>M</i> = 4.92 <i>n</i> = 11 SD = 5.75	ES _s g = 1.53(large) CI[0.59,2.47]	ES _s g = 1.99(large) CI[0.85,3.13]
	WLC	<i>M</i> = 16.74 <i>n</i> = 12 SD = 4.47	<i>M</i> = 15.50 <i>n</i> = 8 SD = 4.87		ES _s g = 0.03 (small) CI [-0.76, 0.82]	
ODSIS	UP	<i>M</i> = 13.83 <i>n</i> = 12 SD = 3.71	<i>M</i> = 5.67 <i>n</i> = 9 SD = 3.39	<i>M</i> = 3.44 <i>n</i> = 9 SD = 4.80	ES _s g = 2.22(large) CI[1.04,3.40]	ES _s g = 2.28(large) CI[1.13,3.44]
	SDP	<i>M</i> = 11.33 <i>n</i> = 15 SD = 4.13	<i>M</i> = 4.22 <i>n</i> = 9 SD = 3.87	<i>M</i> = 2.64 <i>n</i> = 11 SD = 3.67	ES _s g = 2.00(large) CI[0.73,3.26]	ES _s g = 2.41(large) CI[1.14,3.68]
	WLC	<i>M</i> = 10.78 <i>n</i> = 9 SD = 4.41	<i>M</i> = 10.33 <i>n</i> = 6 SD = 5.05		ES _s g = 0.57(medium) CI[-0.06,1.19]	

Note: MDD_CSR = The clinical severity rating from the Anxiety Disorders Interview Schedule (ADIS) for major depressive disorder; Any DD_CSR = The ADIS clinical severity rating for any depressive disorder; HAM-D = Hamilton Rating Scale for Depression; ODSIS = Overall Depression Severity and Interference Scale; UP = Unified Protocol; SDP = Single Diagnosis Protocols; WLC = Waitlist control.

depressive disorder. Results suggest that individuals who received the UP experienced large reductions in symptoms of depression (across clinician-rated and self-report measures) both at the end of treatment and one year following care, compared to baseline levels. Furthermore, descriptive statistics suggest that participants with suicidal ideation (defined as a non-zero response on item 11 of the HAM-D) showed reductions in these symptoms following treatment that were maintained one year later.

Moreover, patients who received the UP experienced significantly lower levels of depressive symptoms at post-treatment when compared to participants on the waitlist on one clinician-rated measure of depressive severity (i.e., HAM-D). Differences in depressive symptoms between the treatment and control groups trended toward significant at the end of treatment on the other two measures included in the study (i.e., ADIS CSR and ODSIS), likely due to the small sample size. As an exploratory aim, we sought to compare effects on depressive symptoms between the UP and gold standard SDPs for anxiety disorders; results suggest that SDP patients demonstrated similar improvements to individuals in the UP condition (though diagnostic severity ratings were greater in magnitude in the UP condition), and clinician-rated and self-reported depression scores were not significantly different as a function of condition at post-treatment or at the 6-month follow-up assessment.

Findings from the present study align with prior research on the effects of transdiagnostic treatments on symptoms of depression and suicidal ideation (Bentley et al., 2017b; Ellard et al., 2010; Farchione et al., 2012; Norton et al., 2004). These results provide further support that the UP may improve depressive symptoms in

individuals with heterogeneous anxiety disorders (Ellard et al., 2010; Farchione et al., 2012). Additionally, consistent with findings from the full sample (Barlow et al., 2017), we found that UP resulted in similar symptom reduction as the SDPs in individuals who met criteria for a depressive disorder. Beyond clinical improvements, transdiagnostic interventions like the UP, may confer dissemination advantages as clinicians need only learn one protocol that is broadly applicable to the majority of their patients (McHugh and Barlow, 2009). Additionally, lower attrition rates in the UP compared to the SDP condition (Barlow et al., 2017) suggest that transdiagnostic interventions may also be more acceptable to patients with comorbid psychopathology.

4.1. Limitations

The conclusions from the current study must be interpreted in the context of its limitations. The present sample was drawn from a study recruiting patients with principal anxiety disorders, which posed two challenges. First, the number of individuals with a depressive disorder was relatively small, resulting in a sample that was underpowered to compare the two active treatment conditions (UP and SDP). Additionally, all participants met criteria for a principal anxiety disorder, limiting our ability to generalize our findings to patients with principal depression; epidemiological data, however, suggests that rates of co-occurrence between anxiety and depressive disorders are quite high (e.g., Kessler et al., 1996). Further limiting generalizability, our sample was predominately Caucasian and college educated, reflecting demographics of our Center; future research should be conducted that

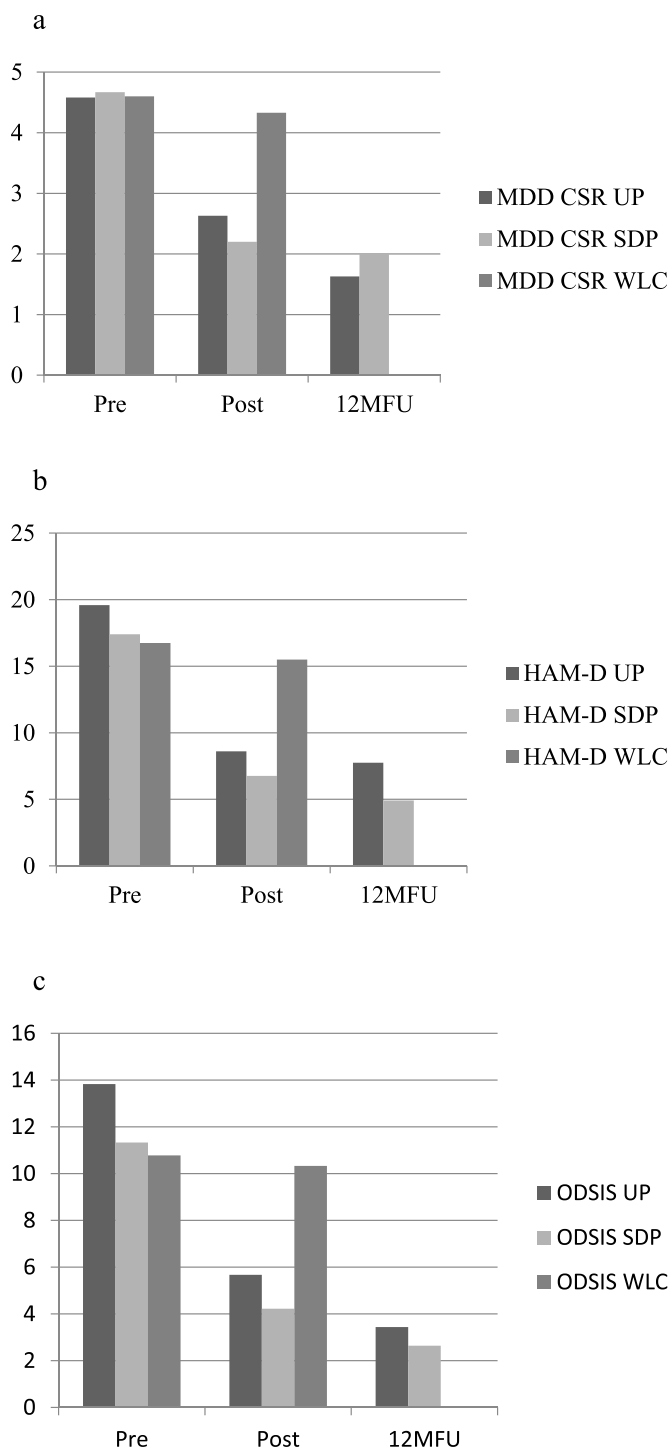


Fig. 1. (a). Average clinical severity ratings (CSR) for major depressive disorder as a function of condition at each timepoint. Pre = Pre-treatment, Post = Post-treatment, 12MFU = 12-month follow-up assessment. UP = Unified Protocol, SDP = Single Disorder Protocol, WLC = Waitlist control condition. (b). Average Hamilton Anxiety (HAM-A) ratings as a function of condition at each timepoint. Pre = Pre-treatment, Post = Post-treatment, 12MFU = 12-month follow-up assessment. UP = Unified Protocol, SDP = Single Disorder Protocol, WLC = Waitlist control condition. (c). Average Overall Depression Severity and Impairment Scale (ODSIS) scores as a function of condition at each timepoint. Pre = Pre-treatment, Post = Post-treatment, 12MFU = 12-month follow-up assessment. UP = Unified Protocol, SDP = Single Disorder Protocol, WLC = Waitlist control condition.

includes individuals from diverse racial, ethnic, and socioeconomic backgrounds. Finally, full analyses were not conducted on the occurrence of suicidal ideation in the sample due to low base rates of these experiences among participants.

4.2. Clinical implications and future directions

The UP offers a transdiagnostic, streamlined approach to the treatment of emotional disorders, and may allow for more effective dissemination of empirically-supported treatments to more clinicians, and in turn provide greater access to these services for patients. Future studies evaluating transdiagnostic CBT for treatment of depression are needed in larger, more diverse (e.g., severity of clinical presentation, race/ethnicity, socioeconomic status, education) samples of individuals. Additionally, future research should actively recruit individuals presenting with principal depression and clinically significant suicidal thoughts to participate in randomized-controlled trials comparing the UP to existing treatments.

CRedit authorship contribution statement

Shannon Sauer-Zavala: Data curation, Formal analysis, Writing - original draft, Writing - review & editing. **Kate H. Bentley:** Writing - original draft. **Stephanie Jarvi Steele:** Writing - original draft. **Julianne Wilner Tirpak:** Writing - original draft. **Amantia A. Ametaj:** Writing - original draft. **Maya Nauphal:** Writing - original draft. **Nicole Cardona:** Writing - original draft. **Mengxing Wang:** Data curation, Formal analysis, Writing - original draft. **Todd J. Farchione:** Funding acquisition, Project administration, Writing - original draft. **David H. Barlow:** Funding acquisition, Project administration, Writing - original draft.

Declaration of Competing Interest

Drs. Barlow, Farchione, and Sauer-Zavala receive royalties from Oxford University Press for their work on the Unified Protocol, the treatment manual under study in the present manuscript. The additional authors declare that they do not have any conflicts of interest.

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Supplementary materials

Supplementary material associated with this article can be found, in the online version, at [doi:10.1016/j.jad.2019.11.072](https://doi.org/10.1016/j.jad.2019.11.072).

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